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EPIDEMIOLOGICAL STUDY OF ABNORMAL BCG SCARS AMONG PRIMARY AND HIGH SCHOOL PUPILS IN TAIWAN(CHINA)[1]

Part 1. Incidence of Abnormal BCG Scars in Relation to Various Background Factors

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INTRODUCTION

During the last several years, more and more parents have brought their children to the TB clinics and complained of abnormal BCG scars. Some of them were indeed large enough to cause worries to the children themselves as well as to their parents. For this, the medical officers of the TB centres could help very little except for referring them to dermatologists. Hsing (1) made a survey in Taipei County, Taiwan, in 1962 and claimed that about 10 per cent of the teen-agers who had received BCG vaccination within five years had ugly keloid formation and thus he warned that ".....the resulting keloid formation endangers the prestige of BCG vaccination. Because of these scars it is conceivable that some day people will refuse to be vaccinated even though the vaccination itself gives certain protection against tuberculosis".

However, whether the incidence of keloid formation is as high as 10 per cent as reported by Hsing should be confirmed, because the rate may vary greatly depending on the definition of keloid, the samples examined, and many other factors. Thus, the present study was planned to make an epidemiological investigation on this problem in randomly selected samples in the northern part of Taiwan, hoping that the information thus collected may contribute to the understanding of the pathogenesis of keloid after BCG vaccination apart from the primary purpose of measuring the extent of the problem.

MATERIALS AND METHODS

BCG programme in Taiwan

The BCG programme in Taiwan started in 1951 and by the end of 1968 a little more than ten million vaccinations had been made. The scheme of BCG vaccination aims at three groups of children. The first group is preschool children as early as possible in life. The second and third groups are children at the first and the sixth grade of the primary schools, respectively. Thus, those who missed the vaccination during the preschool age or whose tuberculin reaction has become negative in spite of previous vaccination are vaccinated at the school entrance, and another chance is given at the time of school leaving. Direct BCG vaccination without tuberculin testing has been applied only to infants since 1965.

Study population

In order to follow up the development of abnormal BCG scars at different intervals after BCG vaccination, observation was made of BCG scars among pupils at the third and the fifth grade of the primary schools and the second grade of both the junior and senior high schools- the latter two will be referred to as the eighth and the eleventh grade hereafter. None of the pupils at these grades had been vaccinated without a prevaccination tuberculin test. The survey was limited to the northern part of Taiwan, including Taipei City, Taipei Hsien (county), Yangmingsan District and Keelung City that comprised about one fifth of the population in Taiwan.

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Sampling method

From the operational point of view, a class, instead of an individual, was used as a sample unit. The average number of pupils per class was 50 to 60. Assuming the estimate of 2% for the prevalence rate of keloid, the following number of classes was ramdonly selected from the total for each grade, in order to secure a reasonably small sampling error: 44 out of 1390 for the third grade, 45 out of 1353 for the fifth grade, 74 out of 701 for eighth grade and 63 out of 321 for the eleventh grade. Since only a small number of high schools were exercising co-education, it was so arranged during the sampling that about the same number of male and female students would be selected. A total of 12,313 pupils, 6226 male and 6087 female, were thus examined. The number of pupils by grade was 2671, 2584, 3996 and 3062 for the third, fifth, eighth and eleventh grade, respectively.

Method of survey

One and the same dermatologist made all the examination throughout the study period in 1967/1968 scholastic year. He examined both arms and shoulders of each pupil for BCG and smallpox scars and measured their size. When no smallpox scars were found, he searched for them on both thighs. He was assisted by a public health nurse in recording and keeping the children in order. A survey card was designed and used in the survey. After the survey, all the cards were sorted and tabulation made by the International Business Machine (IBM), Taipei.

Diagnostic criteria of abnormal BCG scars

The following criteria of keloid, hypertrophic scar and atrophic scar were used in this survey:

1) Keloid:

An elevated hard or elastic firm mass which has at least one of the following three characteristics:

(1) Having projections like crab claws; (Photo. 1)

(2) Larger than the original scar; (Photo. 2)

(3) Teleangiectasis and tense red margin (Photo. 1)

In addition, presence of either one or both of the following characteristics is regarded as supportive of keloid:

(4) Still growing;

(5) Itchy or painful sensation.

2) Hypertrophic scar: (Photo. 3)

An elevated hard or elastic firm mass which has none of the above mentioned three main characteristics.

3) Atrophic scar:

A scar which is depressed from the normal skin and in which the skin appendages have disappeared.

RESULTS

Number of BCG scars

The percentage distribution of the total of 12,313 pupils by number of BCG scars and grade is shown in Table 1. Although the proportion of pupils without BCG scar did not differ very much by grade, the pupils at both eighth and eleventh grades showed a larger proportion with two or more scars than those at the third and fifth grades. This is obviously due to the additional chance of revaccination provided at the sixth grade of primary schools.

Pupils with abnormal BCG scars

As seen in Table 2, there were 10,011 pupils with one or more BCG scars, about half of each sex. Of those, 2,799 or 28.0% had one of the three types of abnormal BCG scars including 46 with two different types of abnormal scars at the same time. Out of these 46 pupils, 6 had an atrophic and a hypertrophic scar and arbitrarily grouped into the hypertrophic scars; 40 had a hypertrophic scar and a keloid and grouped into the keloid in Table 2.

Table 1. Percentage Distribution of Pupils by Number of BCG Scars and Grade

Grade		Without BCG scar	With BCG scars					Total
			One	Two	Three	Four	Five	
3rd	No.	544	1,652	440	32	3	—	2,671
	%	20.4	61.8	16.5	1.2	0.1	—	100.0
5th	No.	552	1,665	319	41	7	—	2,584
	%	21.4	64.4	12.3	1.6	0.3	—	100.0
8th	No.	624	1,755	1,444	149	23	1	3,996
	%	15.6	43.9	36.1	3.7	0.6	0.0	99.9
11th	No.	582	1,436	889	136	19	—	3,062
	%	19.0	46.9	29.0	4.4	0.6	—	100.0
Total	No.	2,302	6,508	3,092	358	52	1	12,313
	%	18.7	52.9	25.1	2.9	0.4	0.0	100.0

Table 2. Prevalence of Pupils with Different Types of Abnormal BCG Scars among Pupils with Scars by Grade and Sex

Grade	Sex	Total No. of Pupils with BCG scars	Pupils with abnormal BCG scars							
			Atrophic scar		Hypertrophic scar		Keloid		Total	
			No.	%	No.	%	No.	%	No.	%
3rd	M	1,103	9(1)*	0.8	183(1)**	16.6	13	1.2	205	18.6
	F	1,024	19(1)	1.9	188(2)	19.4	21	2.1	228	22.3
	Total	2,127	28(2)	1.3	371(3)	17.4	34	1.6	433	20.4
5th	M	1,028	8	0.8	146(2)	14.2	34	3.3	188	18.3
	F	1,004	14	1.4	174(1)	17.3	35	3.5	223	22.2
	Total	2,032	22	1.1	320(3)	15.7	69	3.4	411	20.2
8th	M	1,742	9	0.5	533(11)	30.6	84	4.8	629	35.9
	F	1,630	11(1)	0.7	451(13)	27.7	117	7.2	579	35.5
	Total	3,372	20(1)	0.6	984(24)	29.2	201	6.0	1,205	35.7
11th	M	1,155	10(3)	0.9	249(3)	21.6	60	5.2	319	27.6
	F	1,325	28	2.1	297(7)	22.4	106	8.0	431	32.5
	Total	2,480	38(3)	1.5	546(10)	22.0	166	6.7	750	30.2
Total	M	5,028	36(4)	0.7	1,111(17)	22.1	191	3.8	1,338	26.6
	F	4,983	72(2)	1.4	1,110(23)	22.3	279	5.6	1,461	29.3
	Total	10,011	108(6)	1.1	2,221(40)	22.2	470	4.7	2,799	28.0

* Figures in parentheses show the number of pupils with both atrophic and hypertrophic scars who are arbitrarily included in the "No. of pupils with hypertrophic scar".

** Figure in parentheses show the number of pupils with both hypertrophic scar and keloid who are arbitrarily included in the "No. of pupils with keloid".

Significance tests are made of the difference by age and sex for each type of abnormal BCG scars and all types combined. The results are summarized as below:

Type of scar	Age	Sex
Atrophic scars	P=0.0028 Significant	P is much less than 0.001. Highly significant
Hypertrophic scars	P is much less than 0.001. Highly significant	P is greater than 0.9.
Keloids	P is much less than 0.001. Highly significant	P is much less than 0.001. Highly significant
Total abnormal scars	P is much less than 0.001. Highly significant	P=0.0025 Significant

Age

It appears that the frequency of each type of abnormal BCG scars increases with age, although the case of atrophic scars, which show a fall in frequency until the eighth grade and then rise again, may not be bilogically meaningful. There is however a highly significant, consistent increase in frequency of keloids with age, 0.88 per cent increase per year between the third and eighth grade and 0.23 per cent between the

eighth and eleventh grade. The frequency of hypertrophic scars also significantly increases with age but in an irregular fashion, the average yearly increase being 1.7 per cent.

Sex

Except for hypertrophic scars, there is a highly significant sex difference in frequency for abnormal BCG scars. Although the apparent difference seems small, 0.7 per cent for atrophic scars and 1.8 per cent for keloids, it can be better visualized by noting that for each 100 males with atrophic scars there are 197 females with aprophic scars and for each 100 males with keloids there are 147 females with keloids.

Frequency of abnormal BCG scars in the same persons

Table 3 shows how the chance of having one or more abnormal scars changes with the number of BCG scars in the same person. From the table it appears that the ratio became almost doubled as the number of BCG scars increased to two (40.5%). However, the ratio did not increase further with the increase of the number of BCG scars in the same person.

Those with multiple BCG scars are further analysed by combination of normal and abnormal scars as shown in Table 4. Among the multiple scar group the ratio of having all BCG scars normal was almost the same regardless of the number of BCG scars in the same person (59.5%, 62.0% and 61.5% respectively).

It is also seen that out of the 3,092 pupils with two scars, 13.5% had both scars abnormal. From Table 3 it appears that among persons with only one scar about 21% are abnormal. If the result of a second vaccination among these were to be independent of the outcome of the first vaccination, we should expect

Table 3. Number of Pupils with or without Abnormal BCG Scars by Number of Scars

No. of BCG scars in the same person	Total No. of pupils		Pupils with all scars normal		Pupils with one or more scars abnormal	
	No.	%	No.	%	No.	%
1	6,508	100.0	5,121	79.0	1,387	21.0
2	3,092	100.0	1,837	59.5	1,255	40.5
3	358	100.0	222	62.0	136	38.0
4	52	100.0	33	61.5	19	38.5

Table 4. Distribution of Pupils by Combination of Normal and Abnormal BCG Scars in Groups of Pupils with Multiple BCG Scars

No. of BCG scars in the same persons	Combination of normal and abnormal BCG scars in the same person		No. of pupils	
	Normal	Abnormal	No.	%
2	2	0	1,837	59.5
	1	1	836	27.0
	0	2	419	13.5
Total			3,092	100.0
3	3	0	22	62.0
	2	1	84	23.5
	1	2	33	9.2
	0	3	19	5.3
Total			358	100.0
4	4	0	32	61.5
	3	1	10	19.2
	2	2	7	13.5
	1	3	1	2.0
	0	4	2	3.8
Total			52	100.0

only 21% of these 21%, i.e., 4.4%, to be with the two scars all abnormal, instead of 13.5% as actually observed and shown in Table 4.

For the same token, the expected chance of having all scars abnormal is 0.9% for those with three scars and 0.19% for those with four scars, whereas the observed value is 5.3% and 3.8%, respectively. Thus it could be concluded that one abnormal BCG scar has a good chance of being followed by another from a second vaccination.

Occurrence in the same persons of the same type of BCG scars

In children who have received two or more BCG vaccinations, BCG scars can appear in various combinations of the same or different types. It is important to know whether there is a tendency to develop scars of the same type in children who have received two or more vaccinations. One of the present authors, Woodbury (8), made analysis on this subject, using a multimodal model, and obtained the following conclusion:

BCG scars, either normal or abnormal, appear more frequently in combination of the same type than would be expected if multiple vaccinations are given. In other words, we would expect a certain percentage of combination of scars of the same type under any circumstances but more are found than can be accounted for by chance.

The results of observation on physical characteristics of abnormal BCG scars and the discussion on the problem of abnormal BCG scars will be described in the Part 2 of this report together with the bibliography.

Photo. 1. Keloid after BCG vaccination. Projections like crab claws, teleangiectasis and tense red margin are seen.

Photo.2. Keloid after BCG vaccination. The mass is larger than the original scar which is seen in the centre of the mass.

Photo. 3. Normal BCG scar (right) and hypertrophic scar (left).